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ORIGINAL ARTICLE

The inflammatory response to percutaneous coronary intervention is related to the technique of stenting and not the type of stent

Sherif A. Sakr, Mahmoud M. Ramadan *, Abdelsalam El-Gamal

Department of Cardiology, Faculty of Medicine, Mansoura University, Egypt

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KEYWORDS

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Abstract *Introduction:* Several studies have demonstrated that percutaneous coronary intervention (PCI) induces the release of multiple inflammatory markers which is associated with a later poor prognosis. We aimed to evaluate the inflammatory response to PCI via the assessment of the pre- and post-PCI serum levels of high-sensitive C-reactive protein (hsCRP), interleukin (IL)-6, and intercellular adhesion molecule (ICAM)-1 in relation to the technique of stenting (predilation versus direct stenting [DS]), the type of stent (bare-metal [BMS] versus drug-eluting stents [DES]), the various coronary lesion characteristics, and the other PCI procedural variables.
Methods: We studied 75 consecutive patients (aged 54.2 ± 9.1 years, 54 men) enrolled between March and September 2012. BMS and DES were deployed in 46 and 29 patients respectively; via predilation technique in 37 patients and DS technique in 38 patients. Patients were evaluated monthly in the cardiology outpatient clinic for 6 months.
Results: The procedural increase in hsCRP and ICAM-1 was statistically significant in high risk coronary lesions (total occlusions, bifurcation lesions, and in-stent restenosis). The PCI-induced change of mean hsCRP, IL-6, and ICAM-1 levels was statistically significant in relation to the technique of stenting (predilation leads to augmented inflammatory response compared to DS) but was unrelated to the type of stent (BMS or DES).
Conclusions: Predilation significantly augments the inflammatory response to PCI than DS irrespective of the type of stent (BMS or DES). So, if predilation is required before any type of stent, measures to improve the patient's inflammatory profile should be carried out in advance.

1. Introduction

Several studies have demonstrated that percutaneous coronary intervention (PCI) induces the release of multiple inflammatory markers[1–3] which is associated with poor prognosis[4] and might interfere with the clinical outcome when surgical or

* Corresponding author at: Department of Cardiology, Specialized Medicine Hospital, Mansoura University, Mansoura City, Egypt. Tel.: +20 111 4435751.
E-mail address: amamod2020@yahoo.com (M.M. Ramadan).

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medical treatments are subsequently required.[5] In humans, coronary stents have been shown to elicit an initial acute inflammatory cell response within 0–3 days, centered at the stent struts.[5] The stimulus for the inflammatory process is the disruption of the coronary endothelial layer with a subsequent prompt activation of the inflammatory cells, with early neutrophil recruitment to the site of injury, followed by prolonged macrophage accumulation.[6]

In this study, we aimed to evaluate the inflammatory response to PCI via the assessment of the pre- and post-PCI serum levels of high-sensitive C-reactive protein (hsCRP), interleukin (IL)-6, and intercellular adhesion molecule (ICAM)-1 in relation to the technique of stenting (predilation versus direct stenting [DS]), the type of stent (bare-metal [BMS] versus drug-eluting stents [DES]), the various lesion characteristics, and the other PCI procedural variables.

2. Patients and methods

2.1. Patient selection

We studied 75 consecutive patients enrolled between March and September 2012 from Medicine Specialized Hospital (Mansoura University, Egypt). Patients who underwent coronary stenting in our institution were included in the study unless they met at least one of the following exclusion criteria: left ventricular (LV) ejection fraction $<30\%$, severe heart failure, cardiogenic shock, significant renal impairment (serum creatinine >2 mg/dl), clinical evidence of acute inflammation, malignancy, pregnancy, rheumatic conditions, hepatic decompensation, and treatment with steroids or immunosuppressive drugs.

2.2. Definitions of variables

Hypercholesterolemia was defined as serum total cholesterol (TC) $>$ 200 mg/dl or treatment with lipid-lowering drugs, diabetes as fasting blood glucose level >126 mg/dl on more than 2 occasions or treatment with insulin or oral hypoglycemic drug(s), and hypertension as blood pressure $\geqslant 140/90$ mm Hg on more than 2 occasions or current treatment with antihypertensive drug(s). Current smoking was defined as actively consuming $\geqslant 1$ cigarette/day on the time of admission or in the past year.

Major adverse cardiac events (MACE) were defined as the occurrence of death, acute coronary syndromes (unstable angina or myocardial infarction [MI]), or the need for coronary revascularization (via PCI or coronary artery bypass grafting [CABG] surgery) within a follow-up period of 6 months. In this context, unstable angina was defined as angina pectoris (or equivalent type of ischemic discomfort) with at least one of the following features: (1) occurring at rest (or on minimal exertion) and usually lasting >20 min (if not interrupted by the administration of a nitrate or an analgesic); (2) being severe and usually described as frank pain; or (3) occurring with a crescendo pattern (i.e., pain that awakens the patient from sleep or that is more severe, prolonged, or frequent than previously). Acute, evolving, or recent MI was diagnosed by typical rise and/or fall of biochemical markers of myocardial necrosis with at least one of these criteria: (1) ischemic symptoms; (2) development of pathologic Q-waves in the ECG; (3) ECG changes indicative of ischemia (ST-segment elevation or depression); (4) imaging evidence of new loss of viable myocardium or new regional wall motion abnormality.

2.3. Coronary intervention and sample acquisition

After local anesthesia, a sheath was placed into the femoral artery for insertion of coronary angiography and angioplasty catheters. All patients were pre-medicated with diazepam. Before intracoronary manipulations, an intravenous heparin bolus (80 IU/kg) was administered. A non-ionic contrast medium (Omnipaque, Nycomed Imaging, AS) was used in all processes.

The type of coronary stent, the need for predilation, and final balloon size for stent deployment were chosen by the operators to obtain an angiographic residual stenosis close to zero%. All patients were given aspirin 300 mg and clopidogrel 300 mg before angioplasty.

The PCI procedure was considered successful when the following criteria were fulfilled: (1) post-procedural stenosis $<10\%$ in the worst of 2 orthogonal views with normal contrast run-off in the stented artery, (2) no vascular complications during the procedure, (3) no clinical complications within 48 h after the procedure, and (4) no significant increase in the markers of myocardial necrosis (creatine kinase-MB and troponin-I) 24 and 48 h after the procedure.

After the procedure, the arterial sheath was manually removed when the activated clotting time was <150 s without the use of vascular closure devices; and the patients continued to receive 75 mg/day of aspirin indefinitely and 75 mg/day of clopidogrel for 12 months for DES (6 months for patients with BMS).

Blood samples were obtained within 1 h before and 24 h following PCI after 12 h overnight fasting. The inflammatory response to PCI was defined as the difference between baseline and post-procedural levels of the studied inflammatory marker (calculated as the serum level of the inflammatory marker after the procedure minus its level before the procedure).

2.4. Clinical and angiographic assessment

For follow-up and recording of clinical events, patients were required to visit the cardiac outpatient clinic monthly after the procedure, or when any anginal symptoms occurred. On each visit, the patients were examined clinically, with the addition of a simple exercise test when recommended.

Event-free survival was defined as freedom from MACE. Patients with symptoms or findings suggestive of myocardial ischemia underwent follow-up angiograms. In-segment angiographic restenosis was defined as the loss of $>50\%$ of the initial gain achieved with PCI anywhere within the stent or within the 5-mm borders proximal or distal to the stent.[7]

2.5. Laboratory assessment

Fasting venous blood samples (5 ml each) were obtained from all patients before and 24 h after PCI, and their sera were stored at -70 °C until later assessment for hsCRP, IL-6, and ICAM-1.

Serum levels of ICAM-1 were determined by Enzyme Linked Immuno-sorbent Assay (ELISA) kits obtained from

Ray Biotech Inc. (3607 Bark way Lane, Suite 200, Nor Cross, GA 30092, USA). Serum IL-6 levels were measured by Boster Immune Leader Kit (Boster Biological Technology Ltd., Fremont, CA 94538, USA). Quantitative determination of serum hsCRP was done by immuno-turbidimetric method (Unimate 3 CP, Roche Milan, Italy). The normal upper reference value for hsCRP using this method is 5 mg/L.

Serum fasting glucose level, liver functions, serum creatinine, blood urea nitrogen, and serum electrolytes (sodium, potassium, chloride, and bicarbonates) were measured by automated auto-analyzer (Cobas Integra, Roche, Germany). Full blood count was analyzed by automated cell counter (Sysmex, Roche, Germany). Fasting lipid profile elements (total cholesterol [TC], high-density lipoprotein cholesterol [HDL-C], and triglycerides [TG]) were measured by the standard enzymatic methods; while low-density lipoprotein cholesterol (LDL-C) was estimated by using Friedewald equation (LDL-C = TC – HDL-C – TG/5).

2.6. Statistical methods

Results are represented as mean ± SD for continuous variables and as percentages for non-continuous data. Comparison of percentages was carried out by using χ^2 test. Comparisons of means of continuous data across a grouping variable with 2 or more levels were performed using student's "*t*" and one-way analysis of variance (ANOVA) tests, respectively. A 2-tailed *p*-value <0.05 was considered statistically significant. All analyses were performed using the SPSS statistical software for Windows, version 21 (SPSS Inc., Chicago, Illinois, USA).

2.7. Ethical statement

The study protocol conforms to the declaration of Helsinki, and was approved by our institutional ethical committee. Written informed consent was obtained from all patients prior to their inclusion in the study.

3. Results

This study included 75 patients, 54 (72%) males and 21 (28%) females, aged of 54.2 ± 9.1 years. Table 1 shows the elements of the inflammatory response to PCI, expressed as the difference between pre- and post-PCI levels of high-sensitive C-reactive protein (hsCRP), interleukin (IL)-6, and intercellular adhesion molecule (ICAM)-1, studied in relation to different sets of variables.

3.1. Demographic/history variables

Hypertension was found in 41 patients (54.7%) while 29 (38.7%) were diabetics (13 with type I and 16 with type II), 28 (37%) current smokers, 40 (53%) dyslipidemia, and 32 (42.7%) had positive family history of coronary artery disease (CAD). The patients were maintained on statins ($n = 62$ patients, 83%), aspirin ($n = 71$, 95%), clopidogrel ($n = 58$, 77%), beta-blockers ($n = 39$, 52%), and angiotensin-converting enzyme inhibitors (ACEIs)/angiotensin-receptor blockers (ARBs) ($n = 43$, 57%). There were no statistically significant differences in the magnitude of inflammatory response to PCI (in terms of the 3 studied inflammatory markers) in relation to these demographic/clinical variables ($p > 0.05$ for all comparisons; Table 1).

3.2. Clinical variables

The majority of patients ($n = 34$; 45.3%) presented with stable angina, 29 (38.7%) presented with unstable angina (UA)/non-ST-elevation MI (NSTEMI) and 12 (16%) patients presented with STEMI. Thirty patients (40%) had New York Heart Association (NYHA) class-I dyspnea; and only 5 patients (6.7%) had NYHA class-IV dyspnea. There were no statistically significant differences in the magnitude of inflammatory response to PCI in relation to these clinical variables ($p > 0.05$ for all comparisons; Table 1).

3.3. ECG and Echo variables

Only 8 patients (11%) had normal ECG findings; 30 (40%) had ST-T wave change, and 37 (49%) had pathologic Q-waves. On Echo examination, 27 patients (36%) had diastolic LV dysfunction (21 patients with grade-I and 6 patients with grade-II and higher). There were no statistically significant differences in the magnitude of inflammatory response to PCI in relation to these ECG or Echo variables ($p > 0.05$ for all comparisons; Table 1).

3.4. Coronary lesion variables

Ostial lesions existed in 15 patients (20%); while 12 patients (16%) suffered chronic total occlusions, 33 patients (44%) had bifurcation lesions, and in-stent restenosis was found in 11 patients (14.7%). The majority of coronary lesions belonged to type B1 ($n = 35$; 46.7%), while the least prevalent was type C ($n = 7$; 9.3%); types A and B2 existed in 19 (25.3%) and 14 (18.7%) patients respectively. TIMI-3 flow was observed in 47 patients (62.7%), TIMI-2 in 10 patients (13.3%), TIMI-1 in 6 patients (8%), and TIMI-0 in 12 patients only (16%).

Table 1 demonstrates a statistically significant increase in the magnitude of inflammatory response to PCI (shown by the higher hsCRP and ICAM-1 difference) in patients with chronic total occlusion, bifurcation lesion, and in-stent restenosis. Characteristically, mean IL-6 difference was significantly increased in patients with in-stent restenosis in response to PCI.

3.5. Prognostic variables

A total of 9 MACE occurred in 6 patients (8%) over a follow-up period of 6 months. The events included 1 case with sudden death, 2 cases with MI (one of them as re-infarction), 1 case underwent CABG, and 5 cases underwent revascularization with PCI. There were no statistically significant differences in the magnitude of inflammatory response to PCI in relation to MACE ($p > 0.05$ for all comparisons; Table 1).

3.6. Technique of stenting and type of stent

BMSs were deployed in 46 patients (61.3%); only balloon-expandable, stainless steel, tubular, thin-strut stents with

Table 1 The elements of the inflammatory response to PCI, expressed as the mean difference between pre- and post-PCI levels of high-sensitive C-reactive protein (hsCRP), interleukin (IL)-6, and intercellular adhesion molecule (ICAM)-1, studied in relation to the different sets of variables (using one-way ANOVA and *t*-tests).

Variables	hsCRP difference		IL-6 difference		ICAM-1 difference	
	Mean ± SD	*p*-Value	Mean ± SD	*p*-Value	Mean ± SD	*p*-Value
Demographic/history variables						
Gender						
Male ($n = 54$)	1.72 ± 0.49	0.734	1.75 ± 0.45	0.098	2.15 ± 0.47	0.192
Female ($n = 21$)	1.68 ± 0.35		1.55 ± 0.50		2.30 ± 0.36	
Hypertension						
Present ($n = 41$)	1.68 ± 0.37	0.509	1.86 ± 0.46	0.123	2.13 ± 0.45	0.179
Absent ($n = 34$)	1.75 ± 0.54		1.69 ± 0.48		2.27 ± 0.44	
Diabetes mellitus						
None ($n = 46$)	1.50 ± 0.33	0.531	1.65 ± 0.55	0.729	1.97 ± 0.39	0.176
Type I ($n = 13$)	1.55 ± 0.36		1.57 ± 0.63		2.24 ± 0.51	
Type II ($n = 16$)	1.69 ± 0.47		1.66 ± 0.67		2.29 ± 0.46	
Smoking						
None ($n = 32$)	1.63 ± 0.34	0.380	1.17 ± 0.65	0.123	2.20 ± 0.37	0.976
Current ($n = 28$)	1.78 ± 0.58		2.10 ± 0.48		2.19 ± 0.55	
Ex-smoker ($n = 15$)	1.77 ± 0.36		1.67 ± 0.51		2.20 ± 0.41	
Dyslipidemia						
Present ($n = 40$)	1.70 ± 0.39	0.277	1.78 ± 0.46	0.206	2.29 ± 0.44	0.223
Absent ($n = 35$)	1.59 ± 0.48		1.64 ± 0.49		2.17 ± 0.40	
CAD family history						
Present ($n = 32$)	1.72 ± 0.41	0.329	1.62 ± 0.45	0.466	2.27 ± 0.45	0.216
Absent ($n = 43$)	1.63 ± 0.38		1.70 ± 0.48		2.14 ± 0.44	
Pharmacotherapy						
Statins						
Present ($n = 62$)	1.64 ± 0.44	0.292	1.59 ± 0.49	0.599	2.14 ± 0.47	0.943
Absent ($n = 13$)	1.78 ± 0.39		1.67 ± 0.53		2.13 ± 0.36	
Aspirin						
Present ($n = 71$)	1.61 ± 0.40	0.708	1.65 ± 0.38	0.534	2.09 ± 0.42	0.238
Absent ($n = 4$)	1.69 ± 0.66		1.78 ± 0.79		2.37 ± 0.99	
Clopidogrel						
Present ($n = 58$)	1.59 ± 0.37	0.417	1.62 ± 0.57	0.244	2.13 ± 0.38	0.446
Absent ($n = 17$)	1.68 ± 0.49		1.83 ± 0.87		2.22 ± 0.56	
Beta-blockers						
Present ($n = 39$)	1.75 ± 0.46	0.848	1.74 ± 0.53	0.359	2.17 ± 0.77	0.167
Absent ($n = 36$)	1.77 ± 0.43		1.63 ± 0.50		2.38 ± 0.49	
ACEIs/ARBs						
Present ($n = 43$)	1.71 ± 0.59	0.873	1.69 ± 0.47	0.304	2.27 ± 0.56	0.518
Absent ($n = 32$)	1.69 ± 0.45		1.57 ± 0.53		2.19 ± 0.48	
Clinical variables						
Clinical presentation						
Stable angina ($n = 34$)	1.57 ± 0.63	0.532	1.54 ± 0.55	0.799	2.09 ± 0.39	0.445
UA/NSTEMI < 1 week ($n = 29$)	1.71 ± 0.40		1.82 ± 0.45		2.25 ± 0.41	
STEMI < 1 week ($n = 12$)	1.79 ± 0.36		1.76 ± 0.38		2.19 ± 0.51	
NYHA class						
I ($n = 30$)	1.75 ± 0.47	0.310	1.83 ± 0.39	0.662	2.22 ± 0.36	0.417
II ($n = 22$)	1.69 ± 0.35		1.98 ± 0.37		2.16 ± 0.42	
III ($n = 18$)	1.76 ± 0.31		1.39 ± 0.43		2.44 ± 0.52	
IV ($n = 5$)	1.35 ± 0.41		1.32 ± 0.45		2.09 ± 0.48	
ECG variables						
Normal ECG ($n = 8$)	1.67 ± 0.34	0.212	1.13 ± 0.69	0.495	2.07 ± 0.37	0.226
ST-T wave changes ($n = 30$)	1.83 ± 0.58		1.93 ± 0.71		2.09 ± 0.29	
Q-waves ($n = 37$)	1.63 ± 0.36		1.71 ± 0.61		2.21 ± 0.46	
Echo variables						
LV diastolic dysfunction						
Normal ($n = 48$)	1.64 ± 0.38	0.428	1.81 ± 0.73	0.634	1.98 ± 0.46	0.592
Grade-I ($n = 21$)	1.80 ± 0.60		2.10 ± 0.58		2.18 ± 0.37	
Grade-II and higher ($n = 6$)	1.73 ± 0.62		1.91 ± 0.62		2.24 ± 0.29	

Table 1 (*continued*)

Variables	hsCRP difference		IL-6 difference		ICAM-1 difference	
	Mean ± SD	*p*-Value	Mean ± SD	*p*-Value	Mean ± SD	*p*-Value
Coronary lesion variables						
Ostial lesion						
Present (n = 15)	1.58 ± 0.68	0.364	1.58 ± 0.61	0.852	2.17 ± 0.49	0.880
Absent (n = 60)	1.77 ± 0.73		1.61 ± 0.54		2.15 ± 0.45	
Total occlusion						
Present (n = 12)	1.84 ± 0.54	***< 0.001*** **	1.74 ± 0.56	0.421	2.53 ± 0.52	***0.023*** *
Absent (n = 63)	1.18 ± 0.61		1.59 ± 0.73		2.18 ± 0.47	
Bifurcation lesion						
Present (n = 33)	1.84 ± 0.70	***0.021*** *	1.75 ± 0.54	0.578	2.36 ± 0.53	***0.007*** **
Absent (n = 42)	1.47 ± 0.69		1.69 ± 0.39		2.06 ± 0.41	
In-stent restenosis						
Present (n = 11)	2.00 ± 0.55	***0.014*** *	1.93 ± 0.48	***0.002*** **	2.48 ± 0.40	***0.006*** **
Absent (n = 64)	1.66 ± 0.39		1.53 ± 0.37		2.07 ± 0.45	
Coronary thrombus						
Present (n = 13)	1.68 ± 0.57	0.284	1.76 ± 0.56	0.402	2.10 ± 0.50	0.388
Absent (n = 62)	1.47 ± 0.65		1.57 ± 0.77		2.23 ± 0.44	
Lesion type						
A (n = 19)	1.22 ± 0.71	0.312	1.69 ± 0.57	0.465	1.97 ± 0.36	0.611
B1 (n = 35)	1.45 ± 0.70		1.79 ± 0.36		2.05 ± 0.44	
B2 (n = 14)	1.56 ± 0.63		1.68 ± 0.49		2.00 ± 0.39	
C (n = 7)	1.52 ± 0.66		1.86 ± 0.46		2.08 ± 0.45	
TIMI flow grade						
0 (n = 12)	1.83 ± 0.65	0.930	1.85 ± 0.60	0.879	2.19 ± 0.80	0.648
1 (n = 6)	1.73 ± 0.36		1.63 ± 0.75		2.15 ± 0.73	
2 (n = 10)	1.68 ± 0.49		1.76 ± 0.68		2.31 ± 0.53	
3 (n = 47)	1.86 ± 0.46		1.81 ± 0.54		2.02 ± 0.47	
Prognostic variables						
MACE at 6 months						
Present (n = 6)	1.79 ± 0.51	0.298	1.55 ± 0.47	0.591	2.25 ± 0.43	0.391
Absent (n = 69)	1.62 ± 0.37		1.44 ± 0.59		2.33 ± 0.61	

Abbreviations: ACEIs: angiotensin-converting enzyme inhibitors; ARBs: angiotensin-receptor blockers; CAD: coronary artery disease; ECG: electrocardiogram/electrocardiographic; Echo: echocardiography/echocardiographic; hsCRP: high-sensitive C-reactive protein; IL: interleukin; ICAM: intercellular adhesion molecule; LV: left ventricle/ventricular; MACE: major adverse cardiac events; NSTEMI: non-ST elevation myocardial infarction; NYHA: New York Heart Association; PCI: percutaneous coronary intervention; pts: patients; STEMI: ST elevation myocardial infarction; TIMI: thrombolysis in acute myocardial infarction; UA: unstable angina.

* $p < 0.05$.

** $p < 0.01$.

multicellular design. DES were used in 29 patients (Resolute, Endeavor and Nobori types). In this study, 37 patients (49%) were treated with predilation before stenting and 38 patients (51%) with DS.

Table 2 shows the interaction between the stenting techniques (predilation and DS) and types of stents (BMS and DES); and the resultant impact of this interaction on the inflammatory response to PCI. As shown in the table, there was a statistically significant difference in the magnitude of inflammatory response to PCI in relation to the technique of stenting but not the type of stent; where predilation resulted in an augmented inflammatory response to PCI compared to DS whether BMS or DES were deployed.

4. Discussion

Histological studies have shown that PCI induces a significant inflammatory reaction in the vascular wall with local increases in biochemical markers, leukocyte infiltration, and neointimal hyperplasia.[8,9] The current study showed that the PCI-induced release of hsCRP and ICAM-1 was more pronounced in high risk/complex coronary lesions. Moreover, The PCI-induced increase of mean hsCRP, IL-6, and ICAM-1 levels was not related to the type of stent (BMS or DES) but was rather related to the technique of stenting; where predilation resulted in augmented inflammatory response to PCI compared to DS.

4.1. ICAM-1 as an element of the inflammatory response to PCI

Soluble forms of adhesion molecules (such as sICAM-1, sP-selectin and sE-selectin) have been the aim of several previous studies. The presence of high ICAM-1 values has been communicated in patients with CAD,[10] acute MI[11,12] and UA.[13] Soluble ICAM-1 levels were consistently elevated in patients with acute MI after attempted reperfusion by balloon angioplasty compared with controls and thrombolysed patients.[14] Clinically, significantly elevated soluble ICAM-1 levels were found after PTCA[14] and in the coronary sinus 2 min after PCI, but not in peripheral blood.[11]

Table 2 High-sensitive C-reactive protein (hsCRP), interleukin (IL)-6, and intercellular adhesion molecule (ICAM)-1 in relation to the interaction between stenting techniques and stent types.

Variables	hsCRP difference			IL-6 difference			ICAM-1 difference		
	BMS	DES	*p*-Value	BMS	DES	*p*-Value	BMS	DES	*p*-Value
Predilation	(n = 25) 1.88 ± 0.25	(n = 12) 1.89 ± 0.32	0.877	(n = 25) 2.15 ± 0.15	(n = 12) 2.06 ± 0.18	0.118	(n = 25) 2.38 ± 0.50	(n = 12) 2.56 ± 0.39	0.281
Direct stenting	(n = 21) 1.68 ± 0.38	(n = 17) 1.61 ± 0.41	0.562	(n = 21) 1.86 ± 0.19	(n = 17) 1.88 ± 0.13	0.714	(n = 21) 2.11 ± 0.34	(n = 17) 2.22 ± 0.45	0.396
p-Value	0.037*	0.048*		< 0.001**	0.004**		0.042*	0.044*	

Abbreviations as in Table 1.

4.2. The inflammatory response to PCI in relation to stenting technique

In this study, predilation was associated with statistically significant increase in the mean peri-procedural change of the inflammatory markers (CRP, IL6, and ICAM-1) compared to DS, denoting a more intense inflammatory response with predilation. This result agrees with the findings of Li et al.[15] where SES implantation using DS significantly attenuated the early systemic inflammatory response in patients with single-vessel disease compared with predilation (plasma CRP and IL-6 levels were higher in predilation than in DS group at 24 and 72 h post-stenting). Our study is considered as extension to that of Li et al., as we obtained similar results but with the use of both BMS and DES.

Also, Brasselet et al.[16] showed that the total duration of inflation was related to CRP levels when predilation is used, whereas inflation pressure was not. In contrast, the maximum and average inflation pressures were related to CRP level when DS was used, whereas inflation duration was not. While the study of Brasselet et al. focused only on hsCRP, our study showed that 3 important inflammatory markers (ICAM-1, IL6, and hsCRP) were significantly increased with predilation than with DS.

4.3. The inflammatory response to PCI in relation to the type of stent

The comparative induction of inflammatory response after BMS and DES deployment has been currently evaluated, where the peri-PCI changes of mean hsCRP, IL-6 and ICAM-1 levels were not statistically significant between both types of stents. It was documented that stent type did not influence the change in CRP level, even after adjusting for clinical and anatomic differences observed between groups,[17] in agreement with our findings.

In their randomized trial, Dibra et al.[18] performed serial measurements of hsCRP in the patients who received SES and in those with BMS, and they reported that the median values of hsCRP before and after stenting were similar between both groups, with no statistically significant difference.[18] In another study, a blunted inflammatory response to PCI in terms of reduced CRP peri-procedure ratio was found in subjects with ACS implanted with SES compared to BMS recipients. Karha et al. demonstrated that the increase of hsCRP after PCI was smaller in patients implanted with SES than in those with BMS in a large cohort of patients.[19]

Variability in the magnitude of acute-phase response may be due to a different degree of stent-induced vessel injury and to a different susceptibility to inflammatory stimuli (some patients exhibit hyper-responsiveness to pro-inflammatory damage compared to others). All these considerations might explain the variability and un-predictable inflammatory response elicited by stenting.[2]

The early inflammatory response to PCI was also present after DES deployment which releases substances possessing anti-proliferative and anti-inflammatory activities; indicating the lack of an inhibitory effect of these drugs on the local release of inflammatory mediators in the early post-stenting phase.[20] The effect of these drugs (sirolimus and paclitaxel), although released shortly after stent deployment, is likely to be unable to counteract the endothelial response following the resultant trauma from stent deployment.[20] The acute post-procedural systemic inflammatory response induced by DES appears to be similar to that induced by BMS[7,17,20] in accordance with our results.

4.4. Clinical implications

Our results may indicate that predilation significantly increases the coronary inflammation than DS, irrespective of the type of stent used. Such augmented inflammatory response has been proved to be associated with no-reflow, early and late stent thrombosis and re-stenosis. Thus, if predilation is required before either type of stent (BMS or DES), measures to improve the patient's coronary inflammatory profile should be carried out in advance. Such measures may include the use of high-dose statins,[21] thienopyridines,[22] and glycoprotein IIb/IIIa receptor antagonists.[23]

In an experimental study, liposomes with nitrogen-containing bisphosphonates were administered, which enter the monocytes or macrophages, and then undergo lipolysis with the release of anti-hyperplastic agents preventing cell activation.[24] This approach will be evaluated clinically and may inhibit the cellular proliferation in patients with predominant inflammatory component.

4.5. Limitations

The main limitation of the study is a rather small sample size, and the high prevalence of males is another issue. Also, the enrollment rate in this study is about 3 patients per week; which may denote selection bias. In fact, the weekly rate of coronary interventions in our institute is about 10–12 cases

(divided on 4 days; one day for each team); and we should declare that our team is allowed to include only the cases scheduled in their specified duty day.

As the study is not randomized, there is a potential bias in patients' selection for DS versus predilation technique. However, we should confirm here that the decision to use predilation or DS was largely dependent on the characteristics of the lesion itself and not on the operator's personal preference.

5. Conclusions

From our results, we may conclude that predilation significantly augments the inflammatory response to PCI than DS irrespective of the type of stent (BMS or DES). So, if predilation is required before any type of stent, measures to improve the patient's inflammatory profile should be carried out in advance.

Conflict of Interest

The authors declare that there are no conflict of interests.

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